Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/790,489	**Applicant(s)** FREEHAUF, KEITH ALLAN	
	Examiner Phyllis G. Spivack	**Art Unit** 1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 May 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

June 12, 2008

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614

Continuation of 11. does NOT place the application in condition for allowance because: In the last Office Action it was asserted clear support for each concentration range of the recited ingredients, and the pH range recited in claim 13, is absent in provisional application 60/530939.
Applicant argues recitation of the concentrations of the components is consistent with those recited in the present application. Applicant states though the pH range of component c is not recited as being between 4 and 6 in the '939 application, instruction in claim 11, part c is suggestive of the pH range. In Applicant's view the recitation " a pharmaceutically acceptable amount of a pharmaceutically acceptable stabilizer in an amount effective to decrease the acid or base catalyzed decomposition of at least one avermectin or milbemycin compound" provides guidance sufficient to prepare the claimed premix.
Applicant's argument is not found persuasive. While no examples are required, the pH range is a critical element. The prior art recognized a high degree difficulty and unpredictability in maintaining an adequate shelf life of formulations comprising avermectins and milbemycins. Accordingly, support for the instant compositions and methods within the full scope of the present claims is absent, and the earliest effective date is still determined to be March 1, 2004.

Claims 1, 2 and 4-23 remained rejected under 35 U.S.C. 112, first paragraph, in the last Office Action as containing subject matter that was not described in the specification to provide reasonable enablement for the compositions and methods within the full scope of the claims. Applicant argues enablement is not precluded by the necessity for some experimentation such as routine screening. Applicant urges the adjustment of pH to an acceptable range is readily apparent to one skilled in the art because a list of acceptable acids and/or bases that can be employed is given. An exemplary premix formulation is recited and sufficient direction is given in the specification to generally formulate and improve the stability via the addition of a stabilizer in order to minimize decomposition.
Applicant's arguments are primarily based on hypothetical derminants, i.e., what can be used, can be applied, can be related, and can be achieved, with respect to any stabilizer and avermectin or milbemycin compound. The single working example is drawn to a comparison with and without citric acid (Table II on page 17) under defined storage conditions with respect to temperature and humidity over time (pages 18-20). No results are provided drawn specifically to any other premix formulations wherein a milbemycin or a different stabilizer is employed. Applicant argues sufficient direction is given in the specification to generally formulate and improve the stability via addition of a stabilizer.

The instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success. The rejection under 35 U.S.C. 112, first paragraph, is maintained. Applicant has failed to provide guidance as to other combinations that would reasonably be expected to demonstrate an extension of the shelf life of various avermectins and milbemycins. In view of the industrial problem that is well recognized in the prior art concerning stability of such formulations, the disclosure is not commensurate in scope with the present claims. No direction is provided to distinguish among the various stabilizers that appear to be the most critical element in extending the shelf life of the final product. Accordingly, one skilled in the art would have to test extensively the various pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles, stabilizers and, optionally, at least one insect growth-regulating compound, to discover which particular combination in a premix for an animal feed exhibits an extended shelf-life.

In the last Office Action claims 1, 2 and 4-23 remained rejected under 35 U.S.C. 103(a) as being unpatentable over Beuvry et al., U.S. Patent 5,824,653, in view of Katoh et al., U.S. Patent 4,939,166, Chabala et al., U.S. Patent 4,199,569, Sutherland et al., U.S. Patent 4,910,219, Freehauf et al., U.S. Patent 7,001,889, filed June 21, 2002, and Carson et al., U.S. Patent 6,548,478. It was asserted Beuvry teaches anthelmintic compositions comprising avermectins, milbemycins, or derivatives thereof, and surfactants and stabilizers. The antioxidant, sodium metabisulfite, is encompassed in Example 1. The open language of the present claims allows for the inclusion of any number of additional active or inactive agents. With respect to the requirements of the present claims for pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles and, optionally, insect growth-regulating compounds in animal feed compositions comprising avermectins and milbemycins:
Chabala teaches feed premixes comprising avermectins and milbemycins utilize carriers such as corn meal, citrus meal, fermentation residues, ground oyster shells, wheat shorts, molasses solubles, corn cob meal, bean mill feed, soy grits, dried grains and crushed limestone. Sutherland teaches compositions for veterinary medicine comprising macrolides of formula II may be formulated to include the waxes glyceryl monostearate or coconut oil. Katoh broadly teaches the inclusion of surfactants in a premix for an animal feed comprising macrolide compounds that are structurally analogous to avermectins and milbemycins. Carson teaches the inclusion of anhydrous citric acid in foodstuffs such as feed grain comprising macrolide antibiotics. As required by instant claim 13, the amount should be sufficient to provide a pH of from about 3.0 to about 7.0 in order to minimize the breakdown of the components of the mixture. Freehauf teaches the inclusion of avermectins and milbemycins in oral compositions intended for swine or equine administration, wherein pH stabilizers such as maleic acid or citric acid, antioxidants, such as sodium metabisulfite or ascorbic acid, and surfactants, such as hydrogenated castor oil, are further included.

Applicant argues the priority date of Freehauf is December 25, 2003, while the priority date to which applicants are entitled is December 19, 2003. Applicants further argue Beuvry makes no reference to the control of pH in the formulation. Applicants urge Carson relates to a compound that is functionally and structurally unique from avermectin or milbemycins, and Carson does not relate maintenance of pH to minimization of decomposition. In Applicants' view, unexpected results are presented in Tables II and III of the present application.

Applicant's arguments are not found persuasive. The rejection of record of claims 1, 2 and 4-23 under 35 U.S.C. 103(a) as being unpatentable over Beuvry et al., U.S. Patent 5,824,653, in view of Katoh et al., U.S. Patent 4,939,166, Chabala et al., U.S. Patent 4,199,569, Sutherland et al., U.S. Patent 4,910,219, Freehauf et al., U.S. Patent 7,001,889, and Carson et al., U.S. Patent 6,548,478, is

maintained for the reasons of record. The references collectively teach all limitations of the present claims.

The filing date of Freehauf et al., US Patent 7,001,889, is June 21, 2002. Beuvry teaches the inclusion of "stabilizers" to enhance stability of compositions comprising avermectins and milbemycins in column 2, lines 34-37. The compounds disclosed in Carson are macrolide antibiotics that may be added to feed grain, as a vehicle, and formulated as a premix. Such formulations minimize breakdown and maximize the shelf life of the mixture. See column 3. Virginiamycin, milbemycin and avermectin are all anti-infectives. The characterization of pH maintenance to minimize decomposition is not required. While unexpected results may be set forth in the present application, the results are not commensurate in scope with the instant claims.